VER
Vascular & Endovascular Review

Pecto-Intercostal Fascial Block and Inflammatory Mechanism (TNF-A) in Post-Surgical Heart Pain: a Review Article

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ABSTRACT

Background: Postoperative discomfort subsequent to cardiac surgery predominantly originates from sternotomy and heightened inflammatory activation, characterized by elevated concentrations of tumour necrosis factor-α (TNF-α). The pecto-intercostal fascial block (PIFB) technique has emerged as a potent regional analgesic modality for mitigating sternotomy-related pain and is purported to exert a modulatory influence on inflammatory responses. Objective: This literature review aims to explain the relationship between PIFB, inflammatory mechanisms involving TNF-α, and post-cardiac surgery pain. Results: The literature shows that PIFB can reduce post-sternotomy pain intensity, decrease opioid requirements, and accelerate extubation. Although changes in TNF-α levels vary between studies, there is a scientific basis that facial blocks reduce nociceptor activation and may influence inflammatory pathways associated with TNF-α production. This review integrates the latest findings on PIFB and TNF-α and provides a physiological explanation of the potential relationship between the two in the context of post-cardiac surgery pain. Conclusion: PIFB is an effective analgesic technique with the potential to modulate the inflammatory response, although specific evidence regarding changes in TNF-α is still limited and requires further research.

KEYWORDS: Pecto-Intercostal Fascial Block, TNF-α, Post-Sternotomy Pain, Inflammation, Cardiac Surgery

How to Cite: Fadhiel Yudistiro, Philia Setiawan, Christrijogo Sumartono Waloejo. (2025) Pecto-Intercostal Fascial Block and Inflammatory Mechanism (TNF-A) in Post-Surgical Heart Pain: a Review Article, Vascular and Endovascular Review, Vol.8, No.17s. 307-312.

INTRODUCTION

Postoperative nociception subsequent to cardiac surgery typically manifests at moderate to severe intensities, predominantly attributable to sternotomy incisions, sternal retraction, insertion of thoracic drains, and irritation of musculoskeletal components along with intercostal neural pathways. Empirical investigations indicate that 49% of CABG recipients endure pronounced pain while at rest and up to 78% during coughing episodes on the fourth postoperative day [1]. This nociceptive burden not only diminishes patient comfort, but is also correlated with a spectrum of adverse sequelae, including respiratory compromise, cardiac arrhythmias, delirious states, and an increased propensity for the evolution of persistent chronic pain [2,3].

One important inflammatory mediator involved in the modulation of postoperative pain is TNF-α. This cytokine is known to increase nociceptor sensitivity, trigger hyperalgesia, and play a role in both neuropathic and inflammatory pain mechanisms [4]. In cardiac surgery, TNF-α levels can increase significantly due to surgical trauma and the inflammatory process triggered by the use of cardiopulmonary bypass (CPB) [5]. This makes TNF-α an important indicator in understanding the mechanism of post-operative pain in cardiac surgery.

Conventional analgesic regimens, particularly opioid administration, are frequently employed to ameliorate post-sternotomy discomfort; however, their utilisation is concomitant with a range of untoward effects, including respiratory depression, emesis, ventilator-associated pneumonia, as well as protracted durations of endotracheal intubation and intensive care unit confinement [6–8]. This situation has prompted efforts to develop regional analgesia techniques as a safer and more effective alternative strategy.

One emerging modality is the Pecto-Intercostal Fascial Block (PIFB), a fascial plane blockade directed toward the anterior ramus of the intercostal nerve. This technique has been documented to confer potent analgesic efficacy for sternotomy-induced pain and to attenuate postoperative opioid requirements [9]. In addition to analgesic benefits, some literature suggests that fascial block techniques have the potential to modulate the inflammatory response by reducing peripheral nociceptor stimulation, which theoretically may be associated with a decrease in inflammatory mediators such as TNF-α. Several publications indicate that patients receiving PIFB exhibit better inflammatory profiles and clinical responses, including faster extubation times, although changes in TNF-α levels are not always significant [5,10].

ANESTHESIA BLOCK IN HEART SURGERY

The pecto-intercostal fascial plane block (PIFB), also known as the pecto-intercostal fascial block, is an anaesthesia technique first introduced by de la Torre et al. in 2014 as anaesthesia for breast surgery. However, recent studies have shown that this method can be used to provide anaesthesia during cardiac surgery [11].

Through the dissemination of local anaesthetic agents within the fascial plane, the PIFB induces blockade of the anterior cutaneous branches of the intercostal nerves lateral to the sternal margin across multiple thoracic levels. This intervention demonstrates an analgesic profile comparable to neuraxial techniques and is categorised as a minimally invasive regional anaesthetic modality. As a constituent of the thoracic fascial plane block repertoire, which encompasses the thoracic transversus block, PECS block, and parasternal block, the PIFB is recognised as an integral component of contemporary thoracic regional analgesia [12].

The PIFB procedure has several advantages, including the ability to be performed in the supine position, thereby reducing manipulation or repositioning unlike the paravertebral block (PVB) or erector spinae plane block (ESPB). It can also avoid pleural puncture because the PIFB target location is superficial compared to the thoracic transversus plane block (TTP). Bilateral PIFB only requires one injection on each side, unlike parasternal intercostal blocks that require multiple injections. If performed before incision, bilateral PIFB can be used as intraoperative analgesia, and the use of ultrasound enhances safety by visualising soft tissues, blood vessels, bones, and other nearby structures, allowing direct monitoring of areas to be avoided, such as the pleura or blood vessels [13].

Another salient advantage of PIFB is its capacity to attenuate insulin resistance, suppress systemic inflammatory responses, and diminish postoperative consumption of agents such as sufentanil and parecoxib. Moreover, the technique has been associated with expedited extubation and a reduction in both intensive care unit residency and total duration of hospitalisation.

Postoperative insulin resistance has poor outcomes due to increased incidence of infection, morbidity, mortality, delayed wound healing, and prolonged hospitalisation. PIFB provides control of hyperglycaemia and reduces insulin resistance, thereby decreasing the release of inflammatory mediators [14].

The PIFB technique is executed under real-time ultrasonographic (US) guidance. The US transducer is positioned approximately 2 cm lateral to the midline at the 4th or 5th intercostal interspace to visualise the subcutaneous layers, pectoralis major muscle, intercostal musculature, ribs, pleural interface, and pulmonary structures. Needle advancement is conducted in close proximity to the inferior margin of the transducer, directing the needle tip toward the caudal aspect of the sternum, with its final placement achieved within the fascial interval between the pectoralis major muscle and the external intercostal muscle for deposition of the anaesthetic solution [15,16].

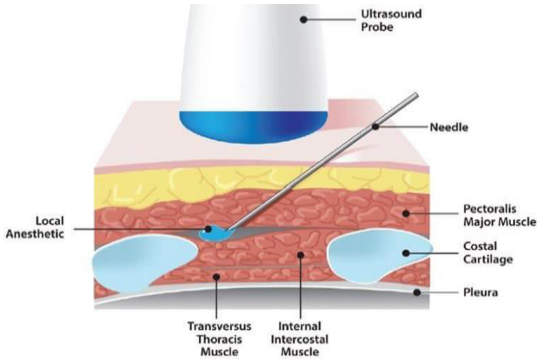

Figure 1: Position of the ultrasound probe and needle during the PIFB procedure [11]

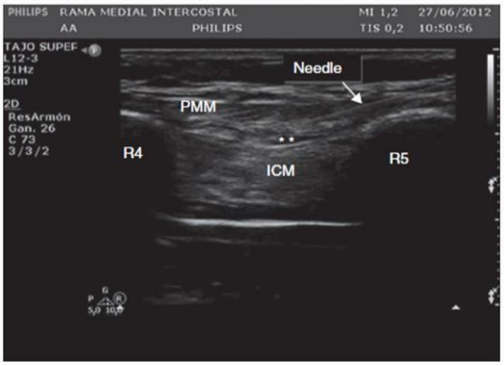

Figure 2: Ultrasound image of PIFB on the anterior chest wall; ICM: intercostal muscles, PMM: pectoralis major muscles, R4: costae 4, R5: costae 5 [16].

MECHANISM OF POST-OPERATIVE PAIN IN HEART SURGERY

All surgical procedures cause pain for patients. Postoperative pain is caused by damage to tissues or organs that occurs during surgery, with the intensity generally corresponding to the degree of damage during surgery [17].

Damage to tissue causes neurogenic inflammation, where the surgical site experiences oedema, redness, and pain [18]. This condition is caused by the release of potassium ions, bradykinin, prostanoids, and other inflammatory mediators such as substance P, serotonin, histamine, cytokines, and leukotrienes. The release of these various mediators causes changes in the sensitivity of terminal afferent nerves, known as peripheral sensitisation. In addition, there is activation of sleeping nociceptors and central sensitisation, which causes an excessive pain response in the surgical wound, known as primary hyperalgesia, and/or in the tissue surrounding the surgical wound, known as secondary hyperalgesia. allodynia, which is a pain response to stimuli that normally do not cause pain, and spontaneous and projected pain [17].

Postoperative nociception arises from irritation of pain receptors, or nociceptors. Transduction within these nociceptors occurs at the peripheral terminals of Aδ and C fibres, where mechanical, thermal, or chemical noxious stimuli are transformed into electrical impulses. These impulses propagate along the nerve fibres toward the dorsal root ganglia via the T2–T6 intercostal nerves and subsequently ascend to the dorsal horn of the spinal cord. From the dorsal horn, the nociceptive signals are relayed through the lateral and medial spinohypothalamic pathways, the spinomesencephalic tract, and the spinulimbic tract before reaching the thalamus, reticular formation, pons, hypothalamus, and periaqueductal grey, ultimately projecting to the cerebral cortex and limbic system. Throughout this transmission cascade, nociceptive input may be either attenuated or potentiated by endogenous modulatory systems, including the opioid, noradrenergic, cholinergic, serotonergic, and γ-aminobutyric acid-ergic networks [17].

In cases of severe trauma, pain is not only superficial and somatic but also visceral, triggered by smooth muscle contraction due to compression and pressure from visceral organs and inflammation [17].

The severity of pain is influenced by the patient's nociception threshold, the location of the surgery, the extent of the surgical procedure, the degree of tissue damage, skin incisions, dissection, sternal retraction, thoracic drainage, endotracheal intubation, sternal wires, the patient's anxiety level before surgery, and the analgesia technique used [17,19].

A study stated that body mass index (BMI) and graft harvesting from the internal mammary artery also have an effect [19,20].

The presence of drains can cause pleuritic pain due to nociceptive impulses from the parietal pleura innervated by the intercostal and phrenic nerves. The degree of trauma to the intercostal nerves when the intercostal space is opened is associated with exacerbation of post-operative pain. Animal studies show that compression of the intercostal nerves during the use of dilators during surgery causes degeneration and demyelination. Damage to the intercostal nerves causes acute and chronic pain characterised by allodynia and/or hyperalgesia, which are indicative of neuropathic pain [17,19,20].

Graft harvesting from the internal mammary artery is significantly associated with postoperative pain because it causes trauma to the internal thoracic cage. Sternum retraction during internal mammary artery harvesting can cause rib dislocation and fracture and cause musculoskeletal pain. Misalignment when returning the sternum can also cause costochondritis [19,20].

High BMI is associated with pain due to surgery in complex obese patients and causes extensive scarring and longer retraction duration during surgery [20]. Patient anxiety before surgery and patient discomfort in the ICU after surgery are associated with post-operative pain [17].

Poorly controlled post-operative pain can cause psychological disturbances in patients [21], such as anxiety, malaise, sleep disturbances, fear, and even depression, and worsen the patient's condition due to systemic sequelae in the form of disturbances in the respiratory and cardiovascular systems, sympathetic stimulation of the nervous system, mobility disturbances, and the patient's physical strength [17].

Pain can cause shortness of breath in patients, reduced tidal volume, vital capacity, functional residual capacity, and lung compliance. The patient's breathing tends to become rapid and shallow. Patients also experience impaired secretion clearance, causing secretions to accumulate in the bronchi and resulting in atelectasis, pulmonary infection, and hypoxaemia [17,19].

Stimulation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis causes rapid heart rate, increased contractility and tone in the heart muscle, increased blood pressure, and hyperglycaemia. This condition can trigger arrhythmias, including atrial fibrillation (AF), and increase oxygen demand in the heart muscle, leading to episodes of ischaemia. Peripheral blood flow decreases, causing venous stasis, which is further exacerbated by immobilisation, leading to deep vein thrombosis (DVT). Disorders also occur in the gastrointestinal tract in the form of motility disorders and spasms in the sphincter, bladder, and urethra [17,19]

In the endocrine system, cortisol, catecholamines, antidiuretic hormone, corticotropin, renin, angiotensin, and aldosterone are released. Conversely, circulating insulin levels decline and a catabolic state ensues. When pain persists over a prolonged duration, immunosuppression develops, thereby heightening susceptibility to infection and disrupting the physiological cascade of wound healing. Platelet aggregability is likewise augmented, accompanied by a proclivity for sodium and water retention. These pathophysiological alterations arise from activation of the sympathetic nervous system, stimulation of the hypothalamic-pituitary-adrenal (HPA) axis, and the release of diverse inflammatory mediators at the locus of tissue injury [17].

Observations indicate that the most severe post-cardiac surgery pain occurs within the first 24 hours after surgery and decreases in

the following days. Pain generally persists for several days to 3 months in some patients. Open cardiac surgery and the use of cardiopulmonary bypass (CPB) cause higher pain intensity. The use of CPB or extracorporeal circulation is associated with a systemic inflammatory response that can cause end-organ dysfunction. Male and elderly patients are reported to have a higher pain threshold [17]. Younger patients experience post-operative pain with higher intensity [1].

TUMOR NECROSIS FACTOR ALPHA (TNF-α)

Tumour necrosis factor-alpha (TNF-α) is a key mediator in pro-inflammatory processes involving necrosis, apoptosis and proliferation. Clinical evidence and experimental studies show that peripheral nerve injury results in the activation and morphological changes of microglia cells in the spinal cord. The regulation that occurs initiates an inflammatory cascade in response to injury. Among the many mediators, TNF-α is recognised as playing a key role in this process, not only modulating the form of the lesion, but also signalling the induction of nociceptive signals [22].

Pain, especially neuropathic pain, is characterised by excessive hypersensitivity or hyperalgesia, sensations such as electric shocks or hyperpathia, and nociceptive responses to non-noxious stimuli or allodynia. This type of pain is difficult to treat and, although it does not significantly interfere with patients' quality of life, it places a considerable burden on healthcare costs. Neuropathic pain, conceptually, is a consequence of peripheral nerve damage resulting from increased neuronal excitability due to sensitisation. The location of this process, whether in the peripheral nerves, the central nervous system, or both, emains a subject of debate. A study showed that the levels of pro-inflammatory and immune mediators in neuropathic pain, such as eicosanoids and bradykinins, are not exclusive to damaged cells and can also come from Schann cells and glial cells in the spinal cord, which have the potential to mediate neuropathic pain [23].

Cytokines or molecular mediators implicated in the pathogenesis of neuropathic pain encompass interleukins, interferons, TNF-α, growth factors, and chemokines. TNF-α functions as a protein ligand for the tumour necrosis factor receptor family (TNF/TNFR). Structurally, TNF-α possesses a trimeric, symmetrical configuration known as the TNF homology domain (THD), which exhibits affinity for all TNF protein subclasses. The THD interacts with TNF receptors, either constitutively expressed (TNFR1, p55-R) or inducible under specific conditions (TNFR2, p75-R) [23].

Multiple investigations have demonstrated comparable findings, identifying the presence of TNF-α within both central and peripheral neural tissues following nerve insult. The TNFR1 receptor is expressed in uninjured regions of the spinal cord involved in nociceptive modulation, such as the dorsal horn, although this structure predominantly expresses TNFR2, which lacks regulatory influence over nociceptor activity. Nevertheless, this distribution does not impede the post-injury release of TNF-α following peripheral nerve damage. During peripheral sensitisation, concentrations of TNF-α rise at the lesioned site and subsequently activate p38 and JNK signalling cascades via TNFR1, leading to upregulation of TTX-R sodium channels and VR1 calcium channels, thereby facilitating the production of inflammatory mediators and substance P. Furthermore, TNF-α enhances the activity of N-Methyl-D-Aspartate (NMDA) and AMPA receptors, culminating in depolarisation processes within the dorsal horn and spinal cord during central sensitization [22].

In neuropathic pain conditions, TNF-α is identifiable at the locus of neural injury and exhibits marked up-regulation, with current evidence indicating its localisation predominantly within macrophages and Schwann cells, as demonstrated in nerve biopsy specimens from individuals afflicted with neuropathic pain. Experimental studies in murine models further reveal that TNF-α orchestrates the activation of downstream cytokine cascades, including IL-1, IL-6, and IL-8. TNF-α is likewise recognised as an initiator of apoptosis via the TNFR1 receptor and caspase-dependent signalling pathways. The ensuing apoptotic processes amplify the expression of TNF-α as well as caspase activity, thereby perpetuating a pathological loop that culminates in the manifestation and maintenance of neuropathic pain [23].

TNF-α is activated as a pro-inflammatory cytokine that exerts a critical role within the neuroimmune circuitry of pain and in generalized nociceptive response models. Experimental rodent studies have likewise demonstrated heightened TNF-α concentrations in the hippocampus, locus coeruleus, and red nucleus. Contemporary evidence indicates that TNF-α facilitates the central mechanisms underlying neuropathic pain predominantly via glial-mediated pathways [23].

TNF-α constitutes a pivotal mediator in the inflammatory cascade, with multiple signalling pathways contributing to the amplification of its transcription, translation, and subsequent release. The principal transcriptional regulators of the TNF-α gene promoter are NF-κB and AP-1, both of which represent downstream effector targets of the MAPK protein kinase family and the NF-κB-kinase inhibitor complex (IKK). Suppression of TNF-α secretion can be achieved through local anaesthetic administration, which impedes lipopolysaccharide (LPS)–induced inflammatory activation in leukocytes. Local anaesthetic agents exhibit marked immunomodulatory potency in vitro, both in human T lymphocytes and murine microglial cells. Two mechanistic pathways underpin this effect: inhibition of NF-κB-mediated mRNA expression and disruption of p38 mitogen-activated protein kinase (MAPK) activation. These dual pathways operate concurrently and serve as critical regulators of inflammatory and stress-related responses. In vivo murine studies further demonstrate that local anaesthetics down-regulate Toll-like receptors (TLRs) and attenuate the synthesis of TNF-α cytokines and prostaglandins in human macrophages and mesenchymal stem cells [24].

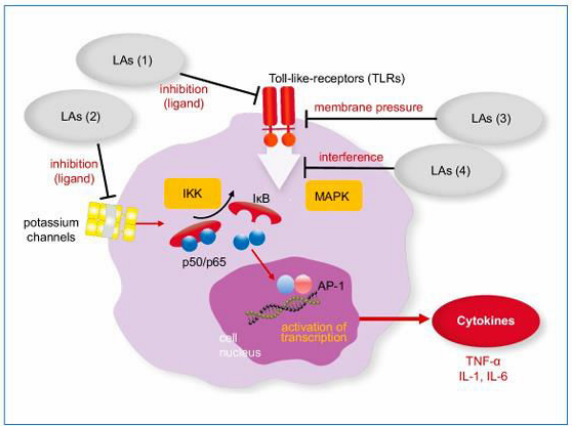

Figure 3: Molecular pathway of TNF-α reduction by local anaesthesia [24]

Elevated TNF-α concentrations may additionally arise from mechanical stressors and the biomolecular consequences of cardiopulmonary bypass (CPB). These perturbations contribute to deterioration in myocardial structural integrity, initiate inflammatory cascades, augment macrophage phagocytic and chemotactic capacity within tissues, and promote systemic dissemination of free radicals via oxidative interactions and apoptosis of cellular substrates. This escalation in TNF-α is most pronounced immediately before and throughout the CPB phase; however, the magnitude of fluctuation is comparatively attenuated relative to the postoperative period [25].

CONCLUSION

Postoperative pain after cardiac surgery is strongly associated with inflammatory activation, particularly the elevation of mediators such as TNF-α. The Pecto-Intercostal Fascial Block (PIFB) technique has been consistently shown across various studies to attenuate post-sternotomy pain, reduce opioid consumption, and improve respiratory function as well as overall recovery time. Although findings regarding changes in TNF-α levels have not been consistent, there is a physiological basis that fascial blocks can reduce nociceptor activation and decrease inflammatory stimuli that may influence TNF-α production. Thus, PIFB offers strong analgesic benefits and the potential for inflammatory modulation; however, clinical evidence regarding its effects on TNF-α requires further investigation.

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